Registratie van ascorbinaatverdunningscurven en van veranderingen in Po2 en bloedstroomsnelheid met onbekende gepolariseerde Pt-elektrodes.

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Summary

Chapter 1.

Indicator dilution technics have found widespread use in cardiovascular research since the routine application of cardiac catherization. The fundamentals of these technics date back to Fick[51a], Stewart[153] and Hamilton[60]. Especially oximetry and dye dilution gained much attention and application. After the introduction of the intravascular Pt-electrode as detector for H_2 and ascorbate by Clark[29,30], these methods drew much interest, a great variety of applications having since been published. Especially the use of inhaled H_2 as indicator and a so-called potentiometric Pt-electrode as detector was used in many investigations, primarily in the evaluation of circulatory shunts. This method however, has the disadvantage of giving only qualitative information. The use of a polarized Pt-electrode for the detection of injected ascorbate as indicator has the benefit of a linear relationship between signal and concentration. The disadvantage of polarized electrodes in a flowing medium is the dependency of the signal on the flow velocity. This drawback limited the application of ascorbate dilution technics, while furthermore most of the available electrodes were, or soon became, insensitive to ascorbate.

Since the beginning of this century the flow dependency of polarized electrodes was known as well as the fact that this dependency decreased under certain circumstances, as described by Nernst[107,108,109]. By using a low polarizing voltage, the reaction of ascorbate and of oxygen at a polarized Pt-electrode can be made to yield a depolarizing current which is virtually independent of the velocity of flow along the electrode. Thus it became possible to record ascorbate dilution curves and oxygen tension variations without pulsatile flow-induced oscillations.

The possibility of recording curves free from flow interference opened a wider field of application for the ascorbate dilution method. Instrumentation and application being very simple, only the development of a variety of electrode catheters and reliable arterial electrodes was necessary. Especially the injection-electrode catheter has become important and the results of the electrode-injection catheter are promising.

The ease and reliability of the developed ascorbate dilution technic for detecting and quantitating circulatory shunts made it possible to increase the field of application outside the catheterization unit, per- and postoperative shunt evaluation becoming feasible. By using the injection-electrode catheter in the out-patient department, quantitive evaluation of recurrent or residual shunts in patients (previously operated upon for ASD II), proved possible.

Using polarized Pt-anodes for the recording of ascorbate dilution curves free from flow interference it became clear that the same flow suppression principle could be used in recording changes in P_{O_2}. O_2 sensitive electrodes also became independent of flow velocity when using a low polarizing voltage. The availability of Pt-electrode catheters with a normal lumen made it possible to record P_{O_2}-changes (ΔP_{O_2}) during sampling or together with pressure variations.

Flow velocity variations (Δv) can be recorded using the flow dependent signal of a Pt-anode polarized with a high voltage. Although this measuring system has the same disadvantages as the measurement with heated thermistors[171] as regards response time, it is now possible to record simultaneously pressure and velocity variations within the circulatory system using only one catheter.

Chapter 2

Although the fundamentals and possibilities of polarized electrodes are described in many textbooks of physical chemistry, a short summary is given. An electrode in a redox system has a potential determined by the concentrations of the oxidized and reduced form of the redox substances, according to the Nernst equation (Eq. 2.1). The redox reaction proceeds forward or backward by applying a voltage to the electrode which differs from the redox potential. The relation between the resulting current and potential is given by Eq. 2.3 and 2.4 and is shown in the polarogram of fig. 2.1. The reaction at the electrode surface can result in a depletion zone around it. In that case the transport of molecules is the limiting factor of the current. The flux of molecules is caused by diffusion and often also by convection.

Flux by diffusion is due to the concentration difference between the electrode surface and the bulk of the solution. Applying Fick's laws[51] for diffusion gives Eq. 2.8. Flux by convection is due to fluid flow or electrode movement. Due to the complexity of hydrodynamics[47,94] the resulting influence on the current can only be approximated. The assumption of a stagnant layer of varying thickness δ_N (Nernst layer), in which the concentration fall is linear (fig. 2.2), makes a mathematical approach possible. The concentration outside the layer remains constant, while the concentration gradient inside the layer is equal to $(c\text{-}c^e)\delta_N$. The current, being proportional to the concentration gradient (Eq. 2.10 and 2.11), thus depends on δ_N.

A high polarizing voltage results in an immediate reaction of all electro-active molecules reaching the electrode. The current is limited by the transport towards the electrode. If the polarizing voltage is so low that not all molecules can react, as in the S-shaped part of the polarogram, the current is determined by the electron transfer coefficient (α) and the reaction rate constant (k_f). In reversible reactions k_f is very large while in irreversible reactions k_f is so low that a greater polarizing voltage is needed to attain the equilibrium as given by the Nernst equation (fig. 2.3). Comparison of the figs. 2.4 and 2.5 shows the influence of k_f on the current in a flowing medium. Ascorbate as well as oxygen react at a polarized Pt-electrode irreversibly, as do most other redox substances[89]. Because k_f depends on the polarizing voltage (Eq. 2.13), the current may become independent of the transport rate towards the electrode at a low polarizing voltage and will be determined by the magnitude of k_f (Eq. 2.14).

The reaction at the electrode itself is preceded and followed by transport of molecules. The total heterogeneous [14,107,133,167] reaction can be separated into 5 single steps.

a. Transport of molecules towards the electrode.
b. Adsorption at the electrode surface.
c. Reaction at the electrode.
d. Release of reaction products.
e. Transport of reaction products.

Steps (a) and (e) are controlled by transport only, (b), (c) and (d) are controlled by the electrochemical process. Since the number of molecules transported (Eq. 2.15) is equal to the number of reacting molecules (Eq. 2.16), the concentration of the reacting molecules at the electrode surface depends only on both rate constants and on the electrode and transport surfaces:

$$c^e = \frac{k_T}{\frac{A_e}{A_T} \cdot k_C + k_T} \cdot c \qquad \text{(Eq. 2.17)}$$

Transport controlled reactions exist when k_C is very large and c^e approaches to zero, as in the plateau of the polarogram. The reaction is chemically controlled when k_C is very small and c^e approaches to c. This also occurs when A_e is much smaller than A_T and k_C in the same order of magnitude as k_T. The current is independent of k_T (Eq. 2.19) for small values of k_C, whereas the current depends on k_T only for large values of k_c. In reactions which are partially or wholly controlled by transport the current is proportional to the thickness of the stagnant layer δ_N. With laminair fluid movement along the electrode, δ_N depends, among others, on the flow velocity (Eq. 2.21).

Suppression of the influence of v on i can be obtained by manipulation of the factors mentioned above. Using a membrane coverage of the electrode keeps the concentration gradient within the nonmoving membrane, when membrane thickness and diffusion coefficient are chosen correctly. The interaction of membrane and fluid parameters are given in Eq. 2.24, identical in form to Eq. 2.17. Using multiple wire or sputtered electrodes results in a very small A_e as compared to A_T.

Using a low polarizing voltage results in a decrease of k_f (Eq. 2.13, 2.14 and 2.19), making k_C small as compared to k_T. In this way an effective suppression of flow effects on bare Pt-electrodes proved possible[115,116].

Recording of blood flow velocity patterns is possible using a high polarizing voltage, resulting in a transport controlled electrode reaction. For this purpose use was made of Pt-anodes, sensitive to ascorbate. The advantage of anodic electrodes above cathodes[101] is the ascorbate concentration of the blood being constant, whereas the oxygen tension varies with respiration. The response time for velocity increase is very short but the reaction on decrease of velocity lasts during the build-up of the new diffusion gradient over the thicker stagnant layer.

Uncovered polarized Pt-electrodes are unstable when used in a biological fluid. At an anode protein and thrombocyte coating is even complicated by erythrocyte coating[52,143]. The decrease in active surface starts immediately after introducing the electrode, calibration thus being impossible. Indirect calibration is stated to be possible for oxygen[76] and hydrogen[83] and even for ascorbate dilution[120].

The latter seems quite doubtfull, because an unknown and changing[182] fraction of the blood ascorbate is in the form of dehydro-ascorbic acid which cannot be detected by the electrode. In the chemical procedure used for calibration[120] however, this unknown quantity is included.

Experiments *in vitro* and *in vivo* were carried out to determine the practical suitability of suppressing flow sensitivity by lowering the polarizing voltage. Fig. 2.8 shows the *in vitro* system to obtain pulsatile flow along the electrode. The polarogram obtained using this set-up is shown in fig. 2.7. Table 2.1 shows the relative flow sensitivity for various values of E_p. The influence of the viscosity (Eq. 2.22) is shown in fig. 2.9. Comparison of fig. 2.10 with fig. 2.5 indicates the irreversibility of the reaction and thus the decrease of the reaction rate when a small polarizing voltage is used. That the same principle holds for membrane covered electrodes[82] is shown in fig. 2.11.

Measurements *in vivo* can also be made insensitive to flow velocity variations as is shown in the figs. 2.12 and 2.13. The linearity of the measuring system has been demonstrated both *in vitro* (fig. 2.14) and *in vivo* (fig. 2.15). The *in vivo* determination is done in dogs under the assumption that the electrode stability and the cardiac output did not alter during the experiment. The electrode was in the dog during $1\frac{1}{2}$ h before the measurement started, the recordings were completed within 40 min.

Chapter 3.

All *in vivo* measurements were made using a circuit[55] the diagram of which is shown in fig. 32, with skin electrodes (fig. 3.6) as reference. The effective polarizing voltage depends on the applied polarizing voltage (E_p) and the active and passive elements between the electrode connections (fig. 3.1).

The unit shown in fig. 3.3 contains the polarizing circuit, a zero-suppression, an active filter circuit and an amplifier. Three different combinations are used for the various clinical applications.

Diagnostic cardiac catheterization: registration of ascorbate dilution curves, oxygen tension variations (ΔP_{O_2}) and velocity patterns together with ECG, respiration[6,140], pressure, dye dilution[68] and/or thermodilution[163]. Oxygen saturation readings were obtained using a CC-oximeter.

Peroperative shunt detection: for this purpose a Pt-electrode was introduced into an internal mammary artery for recording ascorbate dilution curves. In some patients oxygen saturation of caval venous and pulmonary arterial bloodsamples were determined as well.

Shunt detection in out-patients: for this purpose an injection-electrode catheter (fig. 3.5B) was introduced into the pulmonary artery.

To meet the need for reliable electrodes for *in vivo* measurements arterial electrodes as well as special catheters were designed and tested. Because the commercially available arterial electrodes proved to give non-reliable results, other types were constructed. The stiff Pt-electrode (fig. 3.4C) ruled out the electro-chemical short-circuit[89] and has been succesfully used in more than 200 catheterization procedures. The flexible Pt-electrode with a fluid-leakage-preventing-collar around the teflon® insulation (fig. 3.4D) proved reliable and easy to handle. For these reasons this type of electrode is in use since its development (sept. 1967) in all cases of arterial measurements. Intracardiac measurements were mostly carried out using commercially available electrode catheters. They have a Pt-ring around the tip and an open lumen, the connecting wire being embedded in the catheter wall (fig. 3.5A).

The newly developed injection-electrode catheter (IEC)[114,118] has a Pt-electrode at the tip, whereas the lumen ends in 6 injection openings 12-20 cm distal from the tip. Using this catheter only, with the tip situated in the pulmonary artery, it proved possible to evaluate left-to-right shunts. Different methods of construction have been used. The type shown in fig. 3.5B has proved to be the most reliable and is now available commercially.

The injection-thermistor-electrode catheter (ITEC)[117,164] contains a thermistor incorporated in the tip of an injection-electrode catheter (fig. 3.5C). With this catheter it is possible to determine left-to-right shunts (% of $\dot{Q}_p$) with the ascorbate dilution method and pulmonary blood flow (ml. min^{-1}) with the thermodilution method simultaneously.

The electrode-injection catheter (EIC) has 6 lateral openings for injection at the tip and a Pt-electrode 6 cm from the tip (fig. 3.5D). When the tip of the catheter is introduced into the left ventricle, it is possible to record ascorbate wash-out curves to determine the ejection fraction (F_e) of the left ventricle.

The electrode-balloon catheter (EBC) is a Rashkind balloon catheter[129] with a Pt-electrode at the tip (fig. 3.5E). This electrode can be used to record the intracavital ECG and to record oxygen tension variations. A better catheter tip localization is possible using these recordings, while a direct evaluation of the created left-to-right shunt is possible with the ΔP_{O_2}-signal.

All reference electrodes were made of chlorided silver. This gives a stable reference potential and low noise signal[48,57]. For use *in vivo* the reference electrodes (fig. 3.6) are placed on the skin. For central measurements three electrodes are connected and serve as a single reference (fig. 3.7A). Using this "unipolar" reference electrode, the recorded intracavital ECG is interpretable[150,168]. Arterial Pt-electrodes are used with a single reference electrode placed on the homologous extremity (fig. 3.7B and C).

Ascorbate dilution curves are recorded after injection of an amount of 10% Na-ascorbate solution. This solution is prepared with Complexon III and bisulfite to prevent oxidation and with Na-bicarbonate to buffer the solution to pH 7.4. This solution is ampoulated and autoclaved.

The indicator for each dilution curve (0.25 ml) is injected using an injection-block[186] with a syringe having a fixed volume. The indicator is flushed into the circulation with 5-10 ml 5% glucose solution. For peroperative recording of ascorbate dilution curves the indicator is directly injected into the heart with a 0.5 ml syringe and a thin needle. For pulmonary artery injection this needle is introduced via the right ventricular outflowtract.

Chapter 4

Ascorbate dilution curves are comparable to other indicator dilution curves as regards the form of the curve. The normal arterial dilution curve (fig. 4.1A) is followed by a recirculation peak. The normal peak has an exponential downslope[60]. In patients with a right-to-left shunt, the normal peak is preceded by a pre-normal peak, caused by the indicator fraction that shunts to the left and thus reaches the arterial measuring site earlier. In patients having a left-to-right shunt, the normal peak is followed by a post-normal peak caused by the indicator fraction that shunts to the right and thus passes the lung circulation twice before it reaches the measuring site. The curves of fig. 4.2 have been recorded using an injection-electrode catheter with the electrode in the pulmonary artery, the injection openings thus being located in the right atrium or one of the caval veins. The normal curve (fig. 4.2A) shows a better separation between the normal peak and the recirculation peak. In a patient having a left-to-right shunt the curve also shows a post-normal peak better seperated from the normal peak, compare figs. 4.1 and 4.2. Fig. 4.3, recorded using an electrode-injection catheter with the electrode in the aorta and the injection openings in the left ventricle, shows a wash-out curve. The stepwise decrease allows calculation of F_e.

The calculation of shunts from a single dilution curve can be done using various technics. The method as described by Carter proved to be rather insensitive and unreliable[26]. Only shunts which can also be easily evaluated by oximetry, can be determined. The method as described by Mook and Zijlstra proved to be both sensitive and reliable[103]. Shunts down to 5% of the pulmonary blood flow can easily be detected and quantitated. The several peaks of the curve are seperated by semilogarithmic extrapolation of the descending limbs. The magnitude of a left-to-right shunt can be calculated from the areas subtended by the normal and post-normal peaks. In this method the shunted indicator fraction is considered to be a second injection into the heart. A left-to-right shunt Y can be calculated in % of $\dot{Q}_p$. (Eqs. 4.3-4.6). A right-to-left shunt X can be calculated in % of $\dot{Q}_s$. (Eqs. 4.7-4.10). Verification of this calculation has been carried out using simultaneous injection[27] of known amounts of ascorbate (table 4.1) into the right and left atrium, the latter being reached by a transseptal technic. The resulting curves were extrapolated (fig. 4.6) and the simulated shunt calculated using Eq. 4.11. The magnitude of the simulated shunts were also calculated from the injected quantities using Eq. 4.12. The results are given in table 4.2 and fig. 4.7.

The ejection fraction (F_e) of a ventricle (Eq. 4.13) can be calculated[66] from a wash-out curve according to Eqs. 4.14 and 4.15. This technic is mostly carried out using thermodilution. Although the wash-out technic possibly does not give reliable absolute values, it is claimed to be useful in studies with various degrees of cardiac loading[20,58,71,72,164]. Flow independent polarized Pt-electrodes proved suitable to obtain reliable ascorbate wash-out curves. Experiments were performed comparing the ascorbate dilution method with a thermodilution method. The measuring thermistor was therefore situated close to the measuring electrode immediately above the aortic valves. The results are given in table 4.3. To procure information as to ventricular and aortic mixing of indicator and blood, F_e was measured using separate catheters for injection and for measurement. In this way the measuring as well as the injection site could be varied at will. The results, as given in table 4.4, indicate that in the normal dog the site of injection does not influence the F_e measured, while a decrease of F_e is observed when the measuring electrode is at a greater distance from the valves. This decrease is due to additional mixing[99] in the root of the aorta. The use of a single catheter which serves both for injection and detection has the obvious advantage that for the accurate measurement of F_e only one catheter needs be introduced. Moreover the measuring electrode is given a fixed position in the axis of the ejected bloodstream.

Valvular regurgitation can be detected by indicator dilution curves[26,110,179]. Only the upstream sampling technic is able to also give quantitative information[53,148,177,181]. The usefulness of ascorbate dilution compared to other methods was evaluated in dogs with and without mitral regurgitation. Normal closed chest dogs showed a minimal early left atrial appearence of ascorbate injected into the left ventricle (fig. 4.8A). This finding agreed with cine-angiograms obtained using a double-contrast method. In one dog the same determinations were done 14 days after the surgical induction of mitral regurgitation. A clear regurgitation peak is obtained when recording in the left atrium after left ventricular injection. (fig. 4.8A and B). To procure information as to the direct effect of mitral regurgitation, created by chordae incision, recordings were made in an acute experiment before and after the operative interference. The regurgitation curves can be compared to curves obtained after pulmonary artery injection by the same left atrial Pt-electrode. The results are given in table 4.5. The regurgitation fraction is calculated according to Eq. 4.16. An example of the registration is shown in fig. 4.9. In contrast with the findings in the normal, closed chest dog (fig. 4.7A), definitely no regurgitation is shown in the normal dog with open chest (fig. 4.8A).

Recording of intravascular variations in oxygen tension is obtained using a bare Pt-cathode, polarized with $E_p = -400$ mV. The response of such an arterial electrode to one breath of an oxygen enriched gas mixture is shown in fig. 4.10. After 5 h in this position the decrease in sensitivity of the electrode was evaluated. To this end the electrode was withdrawn and cleaned by polishing in the same way as before the first introduction. Part C of fig. 4.11 clearly shows the increase in sensitivity after reintroduction. The sensitivity decreased 9% during the first 10 min; hereafter the decrease is only about 3% per h. The clinical ΔP_{O_2}-recording, being completed within 1 min (Chapter 5), thus will not be influenced by this drift.

Flow velocity variations are recorded using a bare Pt-anode, polarized sufficiently high so that the electrode reaction is transport controlled ($E_p = 1200$ mV). Fig. 4.12 shows the recordings obtained in a dog using a triple-electrode catheter. Two electrodes (AP) and (VCI) are polarized as velocity sensors, the third one (RA) being polarized for ΔP_{O_2}-recording. The inspiratory increase in v_{vci} reaches the pulmonary artery after two cardiac cycles. Fig. 4.13 shows a pulmonary artery velocity pattern together with an intrapleural pressure tracing.

Chapter 5

Detection, localization and evaluation of shunts is especially important in congenital heart disease. Because the correction of these malformations is possible at a lower age now[147], the diagnostic procedures must become simpler and at the same time yield reliable information on a great variety of defects. Moreover, easy, fast and quantitive evaluation of the success of surgical correction of the defects is desirable[106,119,127,160].

During cardiac catheterization ascorbate dilution curves and ΔP_{O_2}-recordings are obtained routinely together with the quantities conventionally measured. Especially in small children the ascorbate dilution technic has the advantage of intravascular detection, avoiding arterial sampling and offering the possibility of varying injection - as well as detection-site at will. The use of the injection-electrode catheter (IEC) makes quantitative evaluation of left-to-right shunts possible without arterial puncture. Fig. 5.1 also shows the possibility of this catheter for the localization of shunts. In patients with an atrial septal defect, the pulmonary detection site proved to be noncritical because mixing is already complete in the right ventricle. In ventricular septal defects some of the shunted blood is ejected by the left ventricle directly into the pulmonary artery. This results in unreliable measurements when the electrode is in the root of the pulmonary artery. Due to additional mixing in the root and bifurcation, correct values are obtained by measurement in one of the pulmonary arterial branches (fig. 5.2).

The reproducibility of shunt determinations using the IEC is given in table 5.1. This table shows series of determinations carried out in 4 patients. Comparison of different methods for the quantitation of shunts show a good agreement (fig. 5.3). As shown by the results of the comparison with data based on oxygen saturation no systematic difference exist between the newly developed and the conventional method. To procure information as to the absolute values of shunts, the IEC was provided with a thermistor for recording of thermodilution curves. Right ventricular output ($\dot{Q}_p$) is calculated from these curves according to Eq. 5.1. Examples of simultaneous recordings are given in figs. 5.4 and 5.5. Shunts can not be detected nor excluded by thermodilution[164], as can be seen by comparing the ascorbate and thermodilution curves.

Right-to-left shunts can only be detected by arterial indicator detection. Even in newborn infants the introduction of the flexible Pt-electrode proved to be easy. Fig. 5.6 shows the good correlation of shunts, as calculated from arterial ascorbate dilution curves, with the results of the conventional methods.

Intravascular P_{O_2}-measurement is possible using membrane-covered electrodes. This method is uptil now not suited for routine application[28,82,91,135]. Using conventional Pt-electrode catheters with a lumen for sampling and pressure recording, it proved possible to reliably record changes in P_{O_2}. The flow sensitivity could be successfully suppressed by lowering the polarizing voltage[115]. During routine use over a 3-year period in more than 350 patients, the method proved very reliable. Only 2 small shunts ($<10\%$ of $\dot{Q}_p$) at ventricular level could not clearly be demonstrated due to the superimposed intracavital ECG. Fig. 5.7 shows the ΔP_{O_2}-recording of an ASD. The typical rise in P_{O_2} is always present when a left-to-right shunt exists. When the catheter is withdrawn along the lateral wall a small shunt sometimes is not shown clearly. Because withdrawal along the medial atrial wall is always possible, no atrial left-to-right shunt need be missed. Fig. 5.8 shows the recordings in 2 cases of PDA. The difference between pulmonary artery and ventricular P_{O_2}-level indicates the difference in shunt magnitude. Fig. 5.9 shows the recordings of a VSD. Sampling at the highest ventricular P_{O_2}-level gave an S_{O_2} of 95%. Fig. 5.10 shows an atrial septal defect right-to-left shunt recording. The left atrial P_{O_2} sometimes nearly reaches the venous P_{O_2}-level. Fig. 5.11 shows P_{O_2}-variations which are synchronous with the respiratory and cardiac cycle. Fig. 5.12 shows right atrial respiratory P_{O_2}-fluctuation due to a respiratory variation in the degree of left-to-right shunting. The inspiratory diminution of the shunt is caused by the increased caval inflow (compare fig. 5.18).

During operative correction of intracardiac shunts, ascorbate dilution curves are recorded using a flexible electrode introduced into an internal mammary artery[119]. Before the correction proper the results are mostly the same as obtained during pre-operative catheterization. Sometimes a defect is found which had not been found previously, in which case the surgical procedure is changed accordingly (fig. 5.13 and 5.14). The recordings of figs. 5.13-5.16 show the scope of the method. The ascorbate dilution method has been routinely used in 84 operations. In 17 patients a residual left-to-right shunt was detected. Three of these could be corrected immediately, 7 proved to be of no hemodynamic importance ($Y<15\%$ of $\dot{Q}_p$), 2 proved to be due to an abnormally draining pulmonary vein ($Y = 13\%$ resp. 8% of $\dot{Q}_p$), one was not corrected because of the poor condition of the patient at that moment. The remaining 4 included one patient with mono-atrium not correctable under hypothermia, one with an incurable Fallot and one with total anomalous pulmonary venous drainage upon which only partial correction was performed because of the left ventricular hypoplasia. The fourth patient had unexpected pulmonary venous drainage of the left lung (fig. 5.13). Correction of this malformation was not possible through the median sternotomy. Fig. 5.15 shows the recording from a patient having an abnormal left coronary artery originating from the pulmonary artery. As is seen in the pre-correction curve, a considerable left-to-right shunt effected the coronary artery steal syndrome[9,138].

Using a single catheter for injection and measurement (IEC) for left-to-right shunt evaluation, it became possible to quantitate shunts in out-patients. Fig. 5.16 shows the results of per- and post-operative evaluation of an ASD residual shunt. Fig. 5.17 shows the resulting curves of a normal patient and of a patient with a residual or recurrent left-to-right shunt. Both patients belonged to a group of 100 patients previously operated upon for the closure of an ASD and controlled afterwards using the described method[144].

The determination of F_e is performed using an electrode-injection catheter (EIC). The results obtained in 3 patients are given in table 5.2. The first patient had aortic stenosis ($P_{lv} = 160/5$ mmHg; $P_{ao} = 105/55$ mmHg), the second patient had mitral stenosis ($MVA = 1.4$ cm^2) and the third patient a hypertrophic obstructive cardiomyopathy on which the effect of Inderal® and Isuprel® was checked. The influence of these drugs on F_e proved to be highly significant.

Flow velocity variations can be recorded applying a high polarizing voltage (+ 1200 mV) to the electrode. As shown in fig. 5.18 the system is too slow to give a reliable velocity pattern; no diastolic plateau is reached. The slower respiratory changes however, can be truly detected (fig. 5.19) and may give information on the inflow of both atria and the influence of intrapleural pressure changes there upon.